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Relationship Between Systemic Lupus Activity Measurement (SLAM) Score and Mortality in Systemic Lupus Erytemathosus (SLE) Inpatients

Hubungan Antara Nilai Systemic Lupus Activity Measurement (SLAM) dan Kematian pada Pasien Lupus Eritomatosus Sistemik (LES)

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ABSTRAK

Latar Belakang: *Lupus Eritomatosus Sistemik (LES) adalah penyakit autoimun kronis yang berat dan mengancam jiwa. Kematian pada LES dapat disebabkan oleh aktivitas lupus atau sequel jangka panjang. Nilai SLAM adalah suatu alat yang dapat mengukur aktivitas penyakit pada pasien penderita lupus.*
Tujuan: *Menganalisa hubungan antara nilai Systemic Lupus Activity Measurement (SLAM) dan mortalitas pada penderita Lupus Eritomatosus Sistemik.*
Metode: *Studi kohort retrospektif dipakai untuk mencapai tujuan penelitian. Penderita Lupus rawat inap dipakai sebagai populasi penelitian. Rekam medis dipakai untuk mengumpulkan data penelitian selama periode 2006-2011. Variabel independen adalah nilai SLAM. Batasan nilai SLAM dibuat berdasarkan rata-rata nilai SLAM (nilai 16.7). Variabel dependen adalah mortalitas.*
Hasil penelitian: *Terdapat perbedaan median survival antara nilai yang kurang dan lebih dari 16.7, yaitu masing-masing 45 and 28 (p 0.034). Terdapat hubungan antara nilai SLAM (lebih dari 16.7) dan HR mortalitas sebesar 2.78 (95% CI 1.028-7.52). Terdapat perbedaan antara jumlah kriteria ACR yang ada, pneumonia, heart rate dengan nilai SLAM (nilai p masing-masing 0.001; 0.001; 0.002). Terdapat perbedaan insiden kematian antara nilai yang lebih dan kurang dari 16.7 yaitu masing-masing 0.35 dan 0.10. Terdapat hubungan antara nilai SLAM (lebih dari 16.7) dengan RR mortalitas sebesar 3.5 (95% CI). Mortalitas pada penderita LES rawat inap adalah sebesar 23%.*
Kesimpulan: *Terdapat hubungan antara nilai SLAM dengan mortalitas penderita lupus yang menjalani rawat inap.*

Kata kunci: *LES, SLAM, kematian*

ABSTRACT

Background: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disorder that can be severe and life threatening. Mortality in SLE may due to lupus activity or long-term sequel. Systemic Lupus Activity Measurement (SLAM) score is a tool that can count lupus disease activity inpatients.
Aims: To analyze the relationship between SLAM score and mortality in lupus inpatients.
Methods: Retrospective cohort study used for reaching objective of the study. Lupus inpatients was used as research population. Medical record was used as study data collection over periods of 2006 until 2011. Independent variable was a SLAM score. The cut point of SLAM score was made based on the mean of SLAM score (16.7 point score). Dependent variable was mortality.
Results: There were differences between number of ACR criteria findings, pneumonia, heart rate with SLAM score (p value 0.001; 0.001; 0.002 respectively).There was a difference of median survival between

less and more than 16.7 point score, 45 and 28 respectively (p 0.034). There was a relationship between SLAM score (more than 16.7 point score) and mortality HR 2.78 (96% CI 1.01-7.53).There was a difference of mortality incidence between more and less than 16.7 point score, 0.35 and 0.10 respectively. There was a relationship between SLAM score (more than 16.7 point score) and mortality RR 3.5 (95% CI). Mortality in lupus inpatients was 23%.
Conclusion: There was a relationship between SLAM score and mortality on lupus inpatients.

Keywords: SLE, SLAM, Mortality

INTRODUCTION

SLE is a multisystem autoimmune disorder characterized by production of several auto antibodies against many spectrums of self-antigen from nucleus, cytoplasm, and surface auto antigen in a predisposing specific genetics that can be severe and life threatening.[1, 2] Mortality in SLE can be caused by disease activity (when major organ or organ system involved), complication of treatment (especially infection), or long term sequel like in cardiovascular diseases.[3] Even in general it has been accepted that high disease activity from time to time will increase risk of organ damage and mortality, only few studies that aimed to scale this association in detail. A cohort study done in University College Hospital (UCH) in 141 SLE patients showed that the average higher British Isles Lupus Assessment Group (BILAG) score associated with organ damage and mortality in the fifth year. Other study in 158 Norwegian lupus patients using Systemic Lupus Erythematous Disease Activity Index (SLEDAI) as disease activity measurement predict that there was an increase Hazard Ratio (HR) of organ damage (SLE Damage Index (SDI) >3) in patients with higher SLEDAI score compared to those with lower SLEDAI score.[4]

Among several systems that can measure SLE disease activity, SLAM is a very good tool. SLAM or SLAM-R (revised) is one of several indices with proven strongest validity that has been used in many researches in many countries with a big scale. SLAM consists of measurement of 24 clinical manifestations, 7 laboratory parameters to evaluate disease activity. Each point have value related to its degree of severity, with total score indicating overall disease activity (higher score indicating more active disease). SLAM includes subjective complain reported by patients and exclude serology/immunology measurement.[5, 6, 7]

This study is aimed to analyze correlation between SLE disease activities measured by SLAM score with mortality in SLE inpatients. Below is the result of study that measure correlation between SLE disease activity with mortality and factors that associate with SLE disease activity in Dr. Sardjito General Hospital Yogyakarta wards.

METHODS

Study Population

Target population in this study was all medical records under ICD X code M 32.9 in Sardjito General Hospital. Reached population were medical records under ICD X code M 32.9 on 2004-2011.

Study Design

This design used retrospective cohort study, by looking to medical records, and then divided into two conditions, died or allowed

to go home (survivor). Data were taken from two groups, exposed and unexposed (control). Exposed group were subjects with high disease activity where as control group were subjects with low disease activity. Periods of study were 30 days. Inclusion criteria were medical records under ICD X code M32.9 that met ACR criteria 1999 for diagnosis of SLE, discharge from hospital due to die or allowed to go home (survivor), medical records can be accessed from medical record installation of Sardjito General Hospital. Exclusion criteria were discharge from hospital by patient intention. Sampling method was consecutive sampling. Number of sample is by total sampling. Independent variable was SLAM score, dependent variable was mortality. Confounding variable were age, age at disease onset, length of illness, gender, treatment with oral methyl prednisolone.

Table 1. Baseline Characteristic Subject

Variable	Result
Age, years	28 ± 9.8
Age < 37 years, n (%)	84 (79.2)
Age > 37 years, n (%)	22 (20.8)
Gender	
Male, n (%)	10 (9.4)
Female, n (%)	96 (90.6)
Length of education, years	10.6± 2.7
<12 years, n (%)	93 (87.7%)
> 12 years, n (%)	13 (12.3%)
Payment methods	
Self finance, n (%)	60 (56.6)
Insurance (*Askes, Jamkesmas, Jamkesda, Gakin*), n (%)	46 (43.4)
Outcome	
Survive, n (%)	82 (77.4)
Dead, n (%)	24 (22.6)
Age at onset	25.75± 10.46
< 40, n (%)	61(57.5)
> 40, n (%)	45 (42.5)
Length of illness, weeks	112.08± 174.58
< 48 weeks, n (%)	64 (59.4)
> 48 weeks, n (%)	43 (40.6)
Hb (g/dl)	8.8± 2.85

RESULT

There were 280 lupus inpatients recorded between 2006 until 2011 under ICD 10 code M 32.9. Only 106 data met the inclusion and exclusion criteria. There were 96 (90.6%) female and 10 (9.4%) male. The mean age was 28 ± 9.8 years. The average of illness was 112.08 ± 174.58 weeks. The average length of education was 10.6 ± 2.7 years. Mean age of disease onset was 25.75±10.46 years. Co morbidities recorded were pneumonia (28.3%), Urinary Tract Infection (UTI) (21.7%). Methods

Table 2. Baseline Characteristic of Subject

Variable	Result
Mcv	74.59± 26.01
Mch	26.32 ± 12.41
Mchc	26.12 ±12.59
Albumin (g/dl)	2.2 ± 1.06
ALT	69.22± 90.05
< 45, n (%)	64 (60.4)
>45, n (%)	42 (39.6)
AST	44.09± 43.83
<40, n (%)	66 (62.3)
>40, n (%)	40 (37.7)
ACR criteria found	
< 5 ACR, n (%)	60 (56.6)
>5 ACR, n (%)	46 (43.4)
Pneumonia, n (%)	30 (28.3)
No pneumonia, n (%)	76 (71.7)
UTI, n (%)	23 (21.7)
No UTI, n (%)	83 (78.3)
ANA	
Negative, n (%)	45 (42.5)
Positive, n (%)	61 (57.5)
Thrombocyte	166858.37 ± 1.55
Leucocyte	8975.38
Anti-dsDNA	
Negative, n (%)	80 (75.5)
Positive, n (%)	26 (24.5)
Use of methyl prednisolone	
<10mg/ day, n (%)	41 (38.7)
>10mg/day, n (%)	65 (61.3)
Heart rate	
< 100 (x/minutes), n (%)	58 (57.4)
>100 (x/minutes), n (%)	48 (45.30)

Table 3. Proportion Difference for Each Variable According to Research Group (Mean Value of SLAM Score: 16,7).

Variable	SLAM score <mean value	SLAM score > mean value	X^2	P value
Number of ACR criteria				
< 5 (n)%	37 (72.5)	23 (41.8)	10.18	0.001
>5 (n)%	14 (27.5)	32 (58.2)		
Co morbidities				
Pneumonia (n)%	44 (86.3)	32 (58.2)	10.29	0.001
Non pneumonia (n)%	7 (13.7)	23 (41.8)		
Heart Rate				
< 100x/ minutes (n)%	36 (70.6)	22 (40.0)	9.99	0.002
> 100 x/ minutes (n)%	15 (29.4)	33 (69.0)		

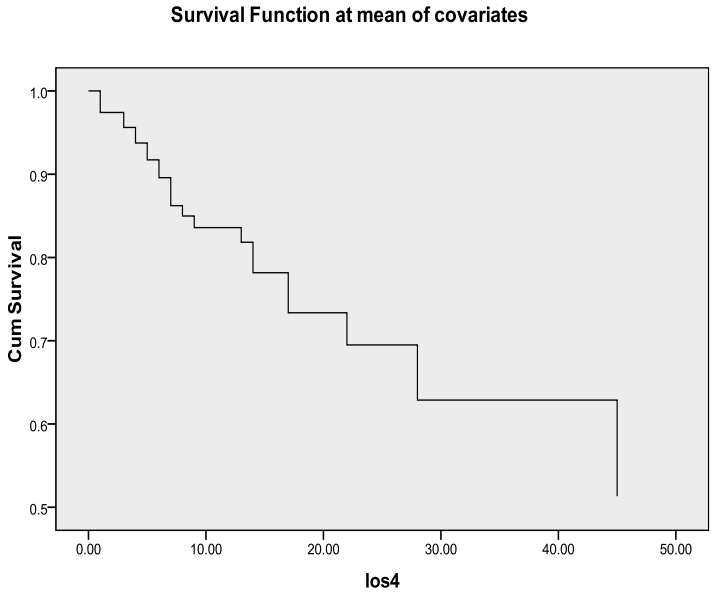

Figure 1. Univariate Analysis.

of payment were by self-finance (56.6%) and insurance *(Askes, Jamkesmas, Jamkesda, Gakin)* (43.4%). Lupus manifestations were hematology (95.3%), renal (76.4%), sororities (62.3%), arthritis (62.3%), positive ANA (57.5%), oral ulcer (56%), discoid rash (55.7%), neuropsychiatry (47.2%), photosensitive (34.6%), positive anti ds-DNA (24.3%), and malar rash (18%).

There were proportion differences in number of ACR criteria >5, pneumonia co morbidity, heart rate > 100/minute in group with SLAM score < mean value and SLAM score > mean value 27.5; 58.2%; 86.3%; 58.2%; 29.4%;69.0% respectively (p value: 0.001).

There were no proportion differences in length of education, age > 32 years, ALT > 45, AST > 40, use of oral MP 10 mg/ day, length of illness > 42 weeks, age of disease onset > 40 years, UTI co morbidity in group with SLAM score < mean value and SLAM score > mean value. The average length of stay in hospital was 12. 5± 11.87 days.

Figure 1 show that the longer length of stay in hospital, the smaller survival rate will be. Analysis was done in all subjects.

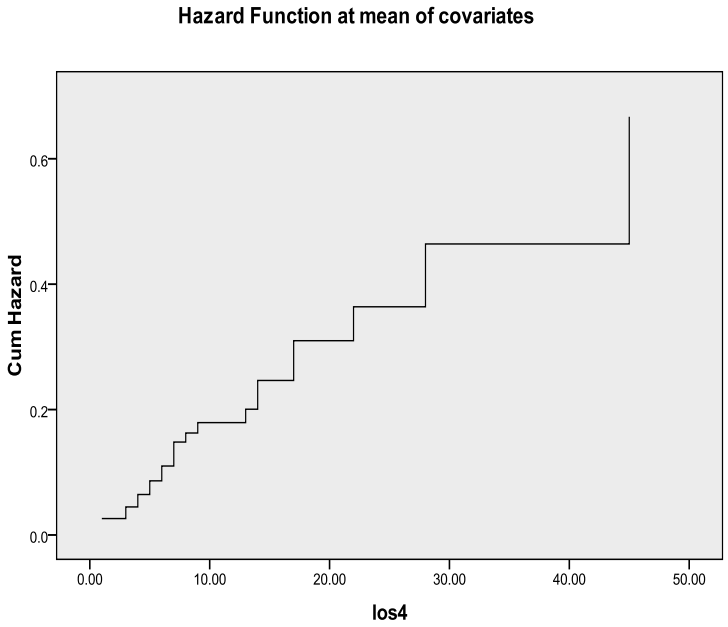

Figure 2. All mortalities according to time function

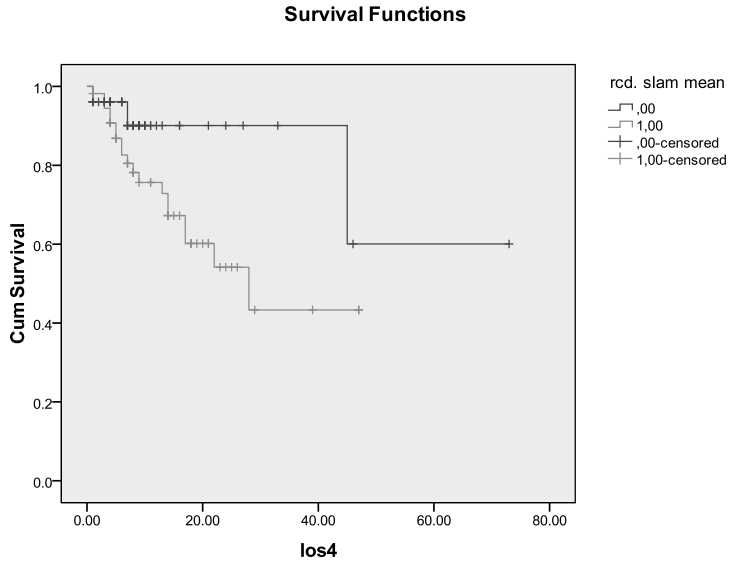

Figure 3. Patients survival according to each group

Figure 2 shows that the longer length of stay, the higher mortality will be. Analysis was done in all subjects.

Figure 3 showed that that the longer length of stay in hospital, the smaller survival rate will be, either in group more than mean value or less than mean value.

Figure 4 shows that the longer length of stay, the higher mortality will be either in group more than mean value or less than mean value.

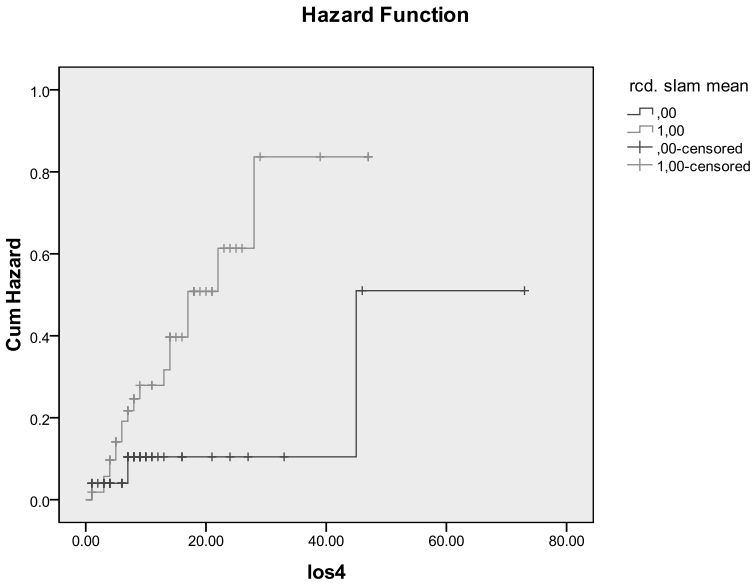

Figure 4. Mortality according to each group

Table 4. Median Survival Rate Were Difference in All Subjects According to High SLAM Score Groups and Low SLAM Score Groups. Variable in Categorical Scale

	SLAM <mean	*SLAM >mean*	X^2	P
Median surviva rate, days	45.00	28.00	4.47	0.034

Median survival rate subjects with SLAM score < mean value was 45 days and subjects with SLAM score >mean value was 28 days. There was a difference of median survival rate between less and more than 16.7 point score, 45 and 28 respectively (p 0.034).

Table 5. The Association between *SLAM* Value and Mortality

	Hazard Ratio	**95% CI**
SLAM >MEAN VALUE	**2.78**	**1.028-7.52**

In this bivariate model analysis, there was an increasing mortality risk in group with SLAM score > than mean value compared to group with SLAM score less than mean value as big as 2.78 HR (95% CI 1.02-7.52)

Table 6. Relative Risk of Mortality between Groups

	Dead	Survive	Total
SLAM>mean value	19(34. 5%)	36 (65.5%)	55 (100%)
SLAM<mean value	5 (9.8%)	46 (90. 2%)	51 (100%)

Mortality incidence in group with SLAM score < mean value was 0.35. Mortality incidence in group with SLAM score > mean value was 0.10. There was increasing mortality risk in groups with SLAM score > mean value compared to SLAM score < mean value as big as 3.5 RR (95% CI). Mortality rate in lupus inpatients was 0.23 (23%).

Table 7. The Association of Confounding Variable and Mortality in Categorial Scale

Variable	*Exp B*	*P value*
Gender	0.00	0.99
Age	0.74	0.25
Age of disease onset	0.71	0.08
Oral methyl prednisolone	3.57	0.02
Length of illness	1.14	0.90

There were no correlation between gender, age, age of disease onset, length of illness with mortality, p value 0.99; 0.25; 0.08; 0.90 respectively. There was a correlation between the use of oral methyl prednisolone > 10 mg with mortality (p: 0.02). Group with the use of oral methyl prednisolone > 10mg had risk 3.57 times higher in mortality compared to group with the use of oral methyl prednisolone < 10 mg.

DISCUSSION

Study conducted in Hospital de Especialidades Centro Medico National (HECMN), Siglo XXI, Instituto Mexicano del Seguro Social showed that between 2004-2006 there were 41 lupus inpatients, mean age was 20±19. Mean length of illness was 21±9 month. Average number of ACR criteria included was 6.5±1.5, 71% skin involvement, 66% articular, 37% cardiopulmonary, 58% renal, 12 % neuropsychiatric, 73% hematology, 95% immunology abnormality (92%, 85%, 17% positive ANA, Anti Ds DNA, Anti-SM respectively).[8] Calvo Alen *et al* found that major manifestations were hematology and musculoskeletal in both research groups.[9] Renal and neurology manifestation significantly more often found in Hispano-American (63.5 and 67.3% respectively) than *Spanish* (33 and 20% respectively) (p=0.0025 and 0.0050).[9]

A longitudinal cohort study in 496 lupus patients found that as many as 98 (19.8%) were Hispanic, 93 (18.8%) Hispanic from Puerto Rico, 172 (34.7%) Afro-American, and 133 (26.8%) were Caucasian. Most population were woman (90.5%), mean age was 35.9 years (SD 12.2), mean length of illness was 17.1 months (SD 16.1), and total length of illness was 63. 1 months (SD. 42.7).[10]

This study consistent with Lopez *et al* (2012) showed that there was increase in mortality as much as 1.15 HR, P =0.007. That study used mean total BILAG score to measure disease activity. In group with the highest quartile of mean total BILAG score had more increase risk of mortality compared to lower mean total BILAG score.[4] Study by Apte *et al* (2008) showed that there was increase in mortality 1.08 *HR*, p= 0.008 in group with SLAM-R score > mean value. This study used mean value of *SLAM-R* for disease activity measurement. Subject with *SLAM* score more than mean value had 1.08 x higher risk in mortality compared to group with lower mean SLAM –R score.[10] Different result showed on study by Teh and Ling *et al*, where disease activity measured by SLEDAI score > 8 was not predictor of mortality in SLE. In that study, infection, flare at admission, SLE Damage Index, LOS, and flare were predictors of mortality with *HR* 9.33; 0.50; 0.92; 0.4 respectively.[11]

CONCLUSION

There were differences between number of ACR criteria findings, pneumonia, heart rate with SLAM score (p value 0.001; 0.001; 0.002 respectively). There was a difference of median survival between less and more than 16.7 point

score, 45 and 28 respectively (p 0.034). There was a relationship between SLAM score (more than 16.7 point score) and mortality HR 2.78 (96% CI 1.01-7.53).

There was a difference of mortality incidence between more and less than 16.7 point score, 0.35 and 0.10 respectively. There was a relationship between SLAM score (more than 16.7 point score) and mortality RR 3.5 (95% CI). Mortality in lupus inpatients was 23%.

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